Secretion

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Secretion is the process of segregating, elaborating, and releasing chemicals from a cell, or a secreted chemical substance or amount of substance. In contrast to excretion, the substance may have a certain function, rather than being a waste product.

Contents

In humans

Secretion in humans include e.g.:

- gastrointestinal tract
  - digestive enzymes
  - gastric acid
- pulmonary
  - surfactant

Mechanism

In humans, just as in all eukaryotic cells, there is a highly evolved process of secretion. Proteins targeted for the outside are synthesized by ribosomes docked to the rough endoplasmic reticulum. As they are synthesized, these proteins translocate into the ER lumen, where they are glycosylated and where molecular chaperones aid protein folding. Misfolded proteins are usually identified here and retrotranslocated by ER-associated degradation to the cytosol, where they are degraded by a proteasome. The vesicles containing the properly-folded proteins then enter the Golgi apparatus.

In the Golgi apparatus, the glycosylation of the proteins is modified and further posttranslational

modifications, including cleavage and functionalization, may occur. The proteins are then moved into secretory vesicles which travel along the cytoskeleton to the edge of the cell. More modification can occur in the secretory vesicles (for example insulin is cleaved from proinsulin in the secretory vesicles).

Eventually, the vesicle fuses with the cell membrane at a structure called the porosome, in a process called exocytosis, dumping its contents out of the cell's environment.[1]

Strict biochemical control is maintained over this sequence by usage of a pH gradient: the pH of the cytosol is 7.4, the ER's pH is 7.0, and the cis-golgi has a pH of 6.5. Secretory vesicles have pHs ranging between 5.0 and 6.0; some secretory vesicles evolve into lysosomes, which have a pH of 4.8.

Nonclassical secretion

There are many proteins like FGF1 (aFGF), FGF2 (bFGF), interleukin1 (IL1) etc which do not have a signal sequence. They do not use the classical ER-golgi pathway. These are secreted through various nonclassical pathways.

Secretory cells

Many human cell types have the ability to be secretory cells. They have a well developed endoplasmic reticulum and Golgi apparatus to fulfill their function.

Secretion in Gram negative bacteria

Secretion is not unique to eukaryotes alone, it is present in bacteria and archaea as well. ATP binding cassette (ABC) type transporters are common to all the three domains of life. The Sec system is also another conserved secretion system which is homologous to the translocon in the eukaryotic endoplasmic reticulum consisting of Sec 61 translocon complex in yeast and Sec Y-E-G complex in bacteria. Gram negative bacteria have two membranes, thus making secretion topologically more complex. So there are at least six specialized secretion system in Gram negative bacteria:

Type I secretion system

It is similar to the ABC transporter, however it has additional proteins that, together with the ABC protein, form a contiguous channel traversing the inner and outer membranes of Gram-negative bacteria. It is a simple system, which consists of only three protein subunits: the ABC protein, membrane fusion protein (MFP), and outer membrane protein (OMP). Type I secretion system transports various molecules, from ions, drugs, to proteins of various sizes (20 - 100 kDa).

Type II secretion system

Proteins secreted through the type II system, or main terminal branch of the general secretory pathway, depend on the Sec system for initial transport into the periplasm. Once there, they pass through the outer membrane via a multimeric complex of secretin proteins. In addition to the secretin protein, 10-15 other inner and outer membrane proteins compose the full secretion apparatus, many with as yet unknown function. Gram-negative type IV pili use a modified version of the type II system for their biogenesis, and in some cases certain proteins are shared between a pilus complex and type II system within a single

bacterial species.

Type III secretion system (T3SS)

It is homologous to bacterial flagellar basal body. It is like a molecular syringe through which a bacterium (e.g. certain types of *Salmonella*, *Shigella*, *Yersinia*) can inject proteins into eukaryotic cells. The low Ca^{2+} concentration in the cytosol opens the gate that regulates T3SS. One such mechanism to detect low calcium concentration has been illustrated by the lcrV (Low Calcium Response) antigen ulitized by *Y. pestis,* which is used to detect low calcium concentrations and elicits T3SS attachment. The Hrp system in plant pathogens inject harpins through similar mechanisms into plants. This secretion system was first discovered in *Y. pestis* and showed that toxins could be injected directly from the bacterial cytoplasm into the cytoplasm of its host's cells rather than simply into the extracellular medium.[2]

Type IV secretion system

It is homologous to conjugation machinery of bacteria (and archaeal flagella). It is capable of transporting both DNA and proteins. It was discovered in *Agrobacterium tumefaciens*, which uses this system to introduce the Ti plasmid and proteins into the host which develops the crown gall (tumor). *Helicobactor pylori* uses a type IV secretion system to deliver CagA into gastric epithelial cells. *Bordetella pertussis*, the causative agent of whooping cough, secretes the pertussis toxin partly through the type IV system. *Legionella pneumophila*, the causing agent of legionellosis (Legionnaires' disease) utilizes type IV secretion system, known as the icm/dot system, to translocate numerous effectors proteins into its eukaryotic host.

Type V secretion system

Also called the autotransporter system,[3] type V secretion involves use of the *sec* system for crossing the inner membrane. Proteins which use this pathway have the capability to form a beta-barrel with their C-terminus which inserts into the outer membrane, allowing the rest of the peptide (the passenger domain) to reach the outside of the cell. Often, autotransporters are cleaved, leaving the beta-barrel domain in the outer membrane and freeing the passenger domain. Some people believe remnants of the autotransporters gave rise to the porins which form similar beta-barrel structures.

Type VI secretion system

Secretion of several proteins by the Type VI secretion system from *Vibrio cholerae* and *Pseudomonas aeruginosa* was recently described.[4][5] Proteins secreted by the type VI system lack N-terminal signal sequences.

Twin-arginine translocation

Bacteria as well as mitochondria and chloroplasts also use many other special transport systems such as the twin-arginine translocation (Tat) pathway which, in contrast to Sec-depedendent export, transports fully folded proteins across the membrane. The name of the system comes from the requirement for two consecutive arginines in the signal sequence required for targeting to this system.

Release of outer membrane vesicles

In addition to the use of the multiprotein complexes listed above, Gram-negative bacteria possess another method for release of material: the formation of outer membrane vesicles.[6] Portions of the outer membrane pinch off, forming spherical structures made of a lipid bilayer enclosing periplasmic materials. Vesicles from a number of bacterial species have been found to contain virulence factors, some have immunomodulatory effects, and some can directly adhere to and intoxicate host cells. While release of vesicles has been demonstrated as a general response to stress conditions, the process of loading cargo proteins seems to be selective.[7]

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See also

- Secretory proteins

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